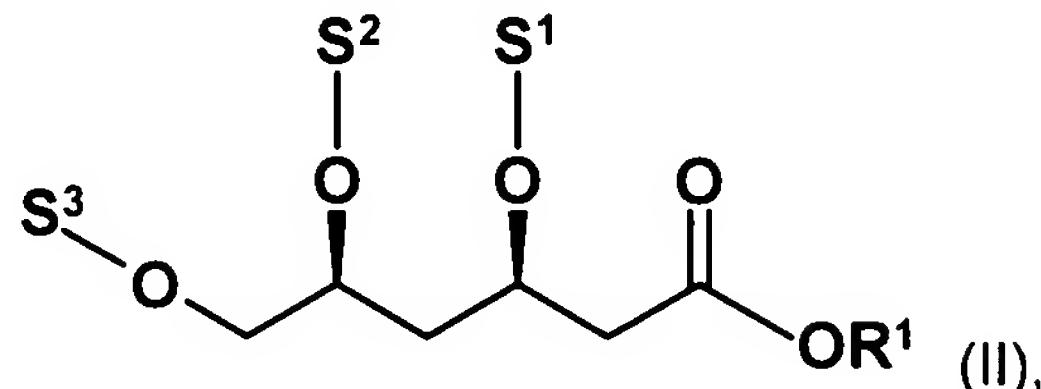


## **Patent claims:**

5

1. Process for the preparation of a statin, comprising the following steps:
  - a) Preparation of a compound of the formula II

10



in which

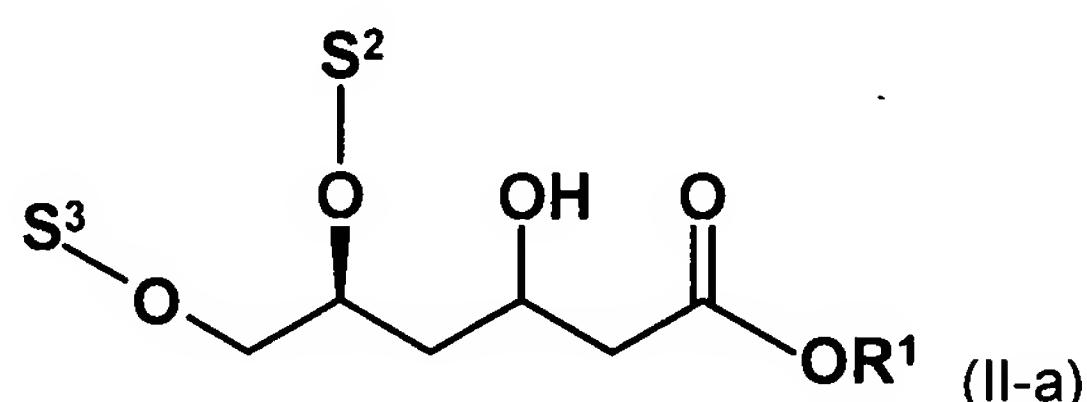
$S^1$  denotes a hydrogen atom or a hydroxyl protective group,  
 $S^2$  and  $S^3$ , independently of one another, denote hydroxyl protective groups and  
15  $R^1$  represents a hydrogen atom or a carboxyl protective group,

by stereoselective hydrogenation of a compound of the formula III

$$\begin{array}{c}
 \text{S}^2 \\
 | \\
 \text{O} \\
 | \\
 \text{S}^3-\text{O}-\text{C}-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{CH}_2-\text{C}(=\text{O})-\text{CH}_2-\text{OR}^1
 \end{array}
 \quad (\text{III})$$

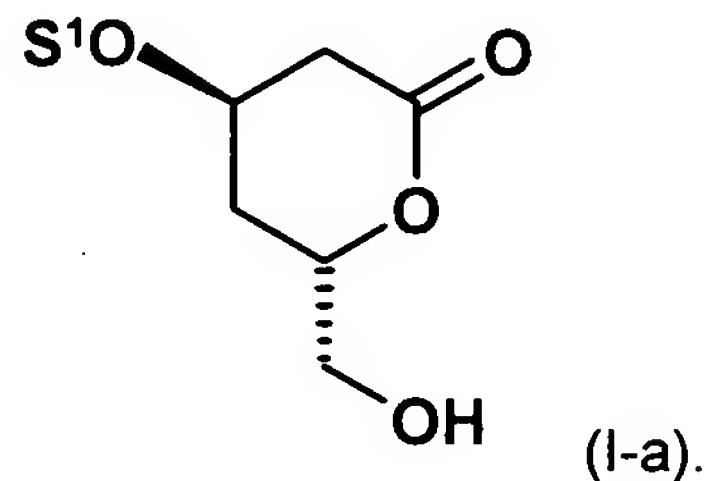
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to give a compound of the formula II-a



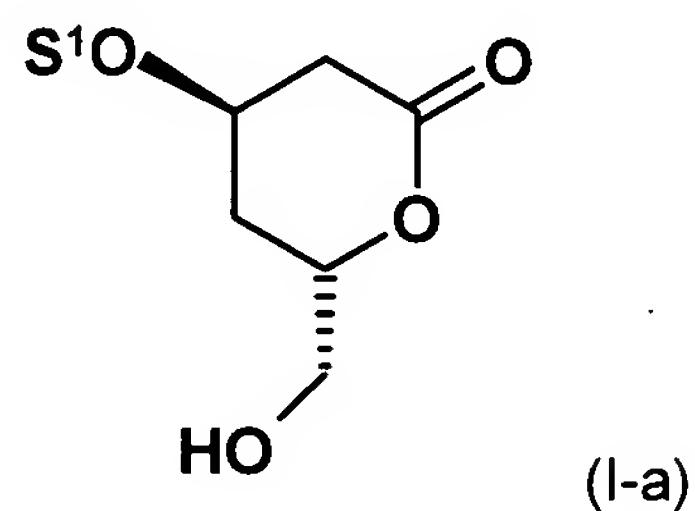
and optionally introduction of a hydroxyl protective group and

b) lactonization of the compound of the formula II to give a compound of the formula I-a



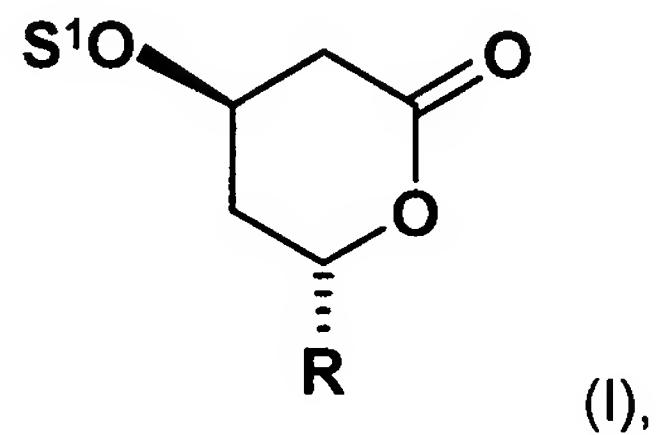
5 2. Process according to Claim 1, comprising the further step

c) conversion of the compound of the formula I-a



10

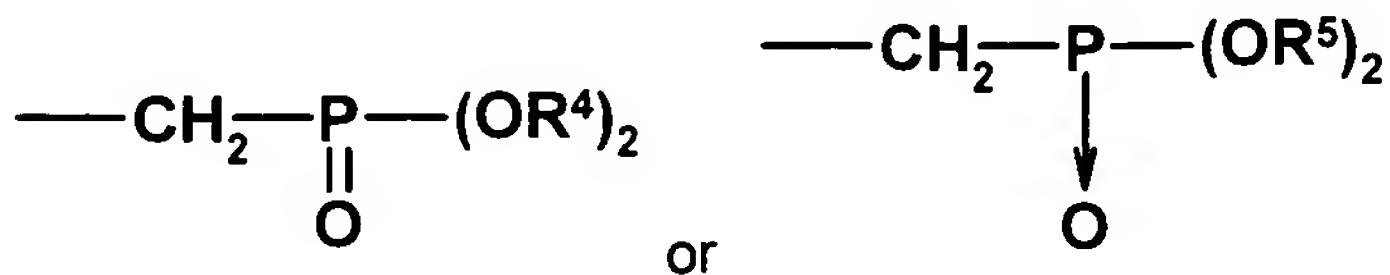
into a compound of the formula I



## 15 where the radical

$S^1$  is as defined in Claim 1,

R denotes  $-\text{CH}_2\text{R}^2$ ,  $-\text{CHO}$ ,  $-\text{CH}=\text{P}(\text{R}^3)_3$ ,  $-\text{CH}_2-\text{P}^+(\text{R}^3)_3\text{M}^-$ ,



$R^2$  denotes a halogen atom,  $-C\equiv N$ ,  $-CH_2NH_2$ ,  $-SO_2-R^6$  or a leaving group,

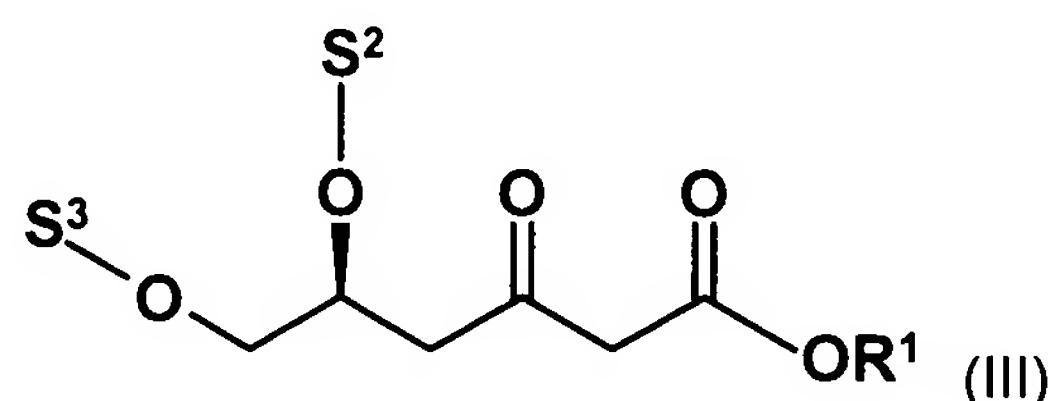
$R^3$ ,  $R^4$  and  $R^5$  complete a Wittig radical or a Horner-Wittig radical,

$R^6$  denotes a hydrogen atom or a  $C_{1-3}$ -alkyl or a  $C_{5-10}$ -aryl radical, which are optionally substituted by one or more radicals which, independently of one another, are selected from halogen atoms, heterocycles which contain 0 to 10 carbon atoms and 1 to 10 heteroatoms selected from sulphur, nitrogen and oxygen atoms, and functional groups and

$M^-$  represents an opposite ion.

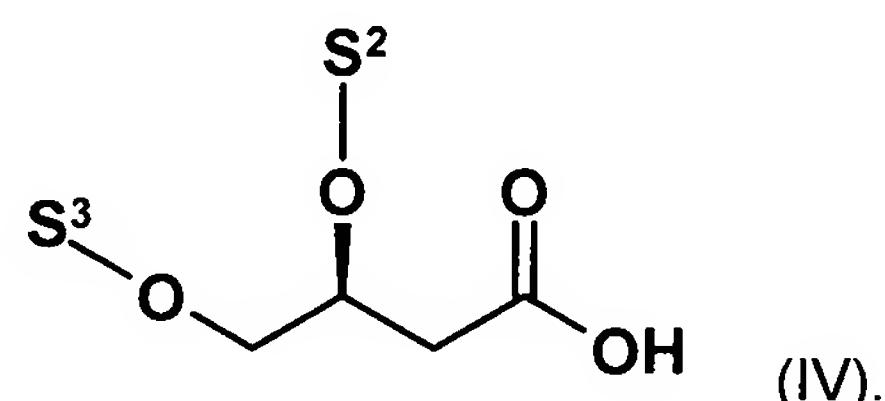
10 3. Process according to Claim 1 or 2, comprising the step:

### preparation of a compound of the formula III



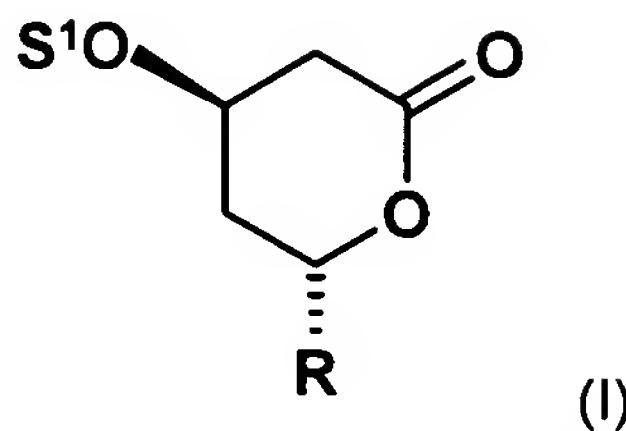
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by chain extension of a compound of the formula IV

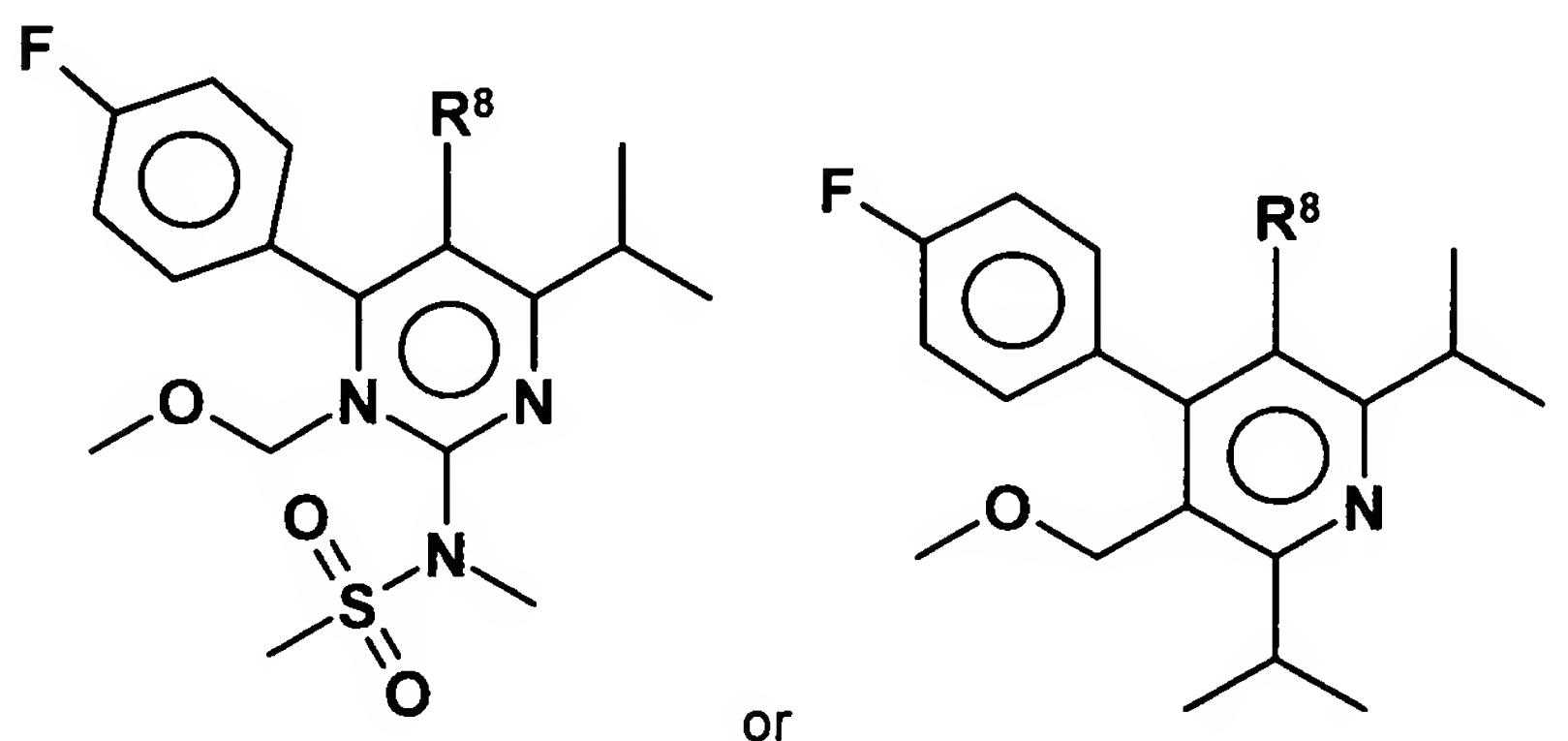
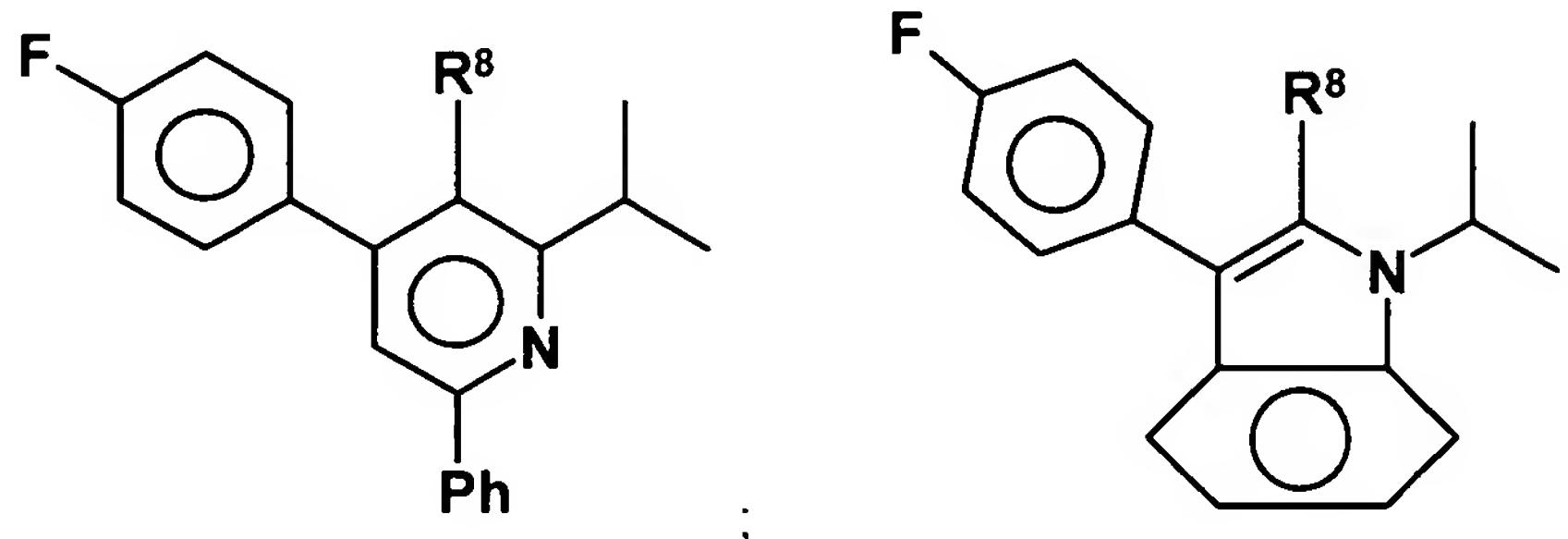


20 4. Process according to any of Claims 1 to 3, the compound of the formula I being converted into the statin by one of the following process steps and then optionally by opening of the lactone ring and optionally by removal of protective groups:

a) reaction of a compound of the formula (I)



in which the radical R represents a CHO group and the radical S¹ is as defined in Claim 1,  
 5 with a compound of the formula

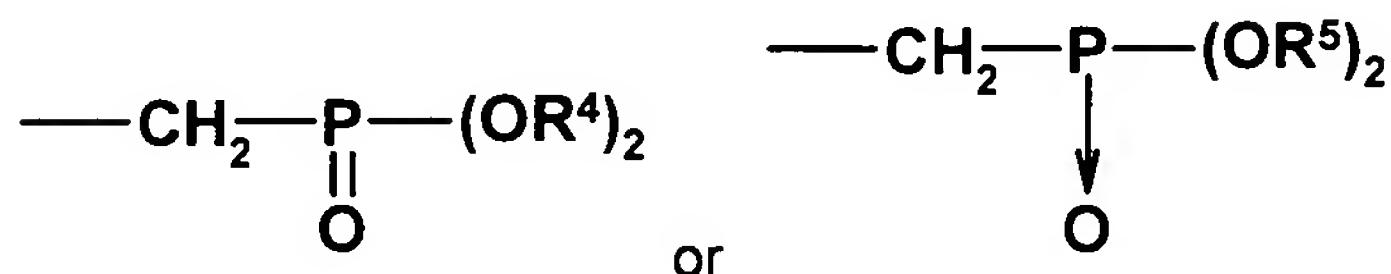


10

or

in which

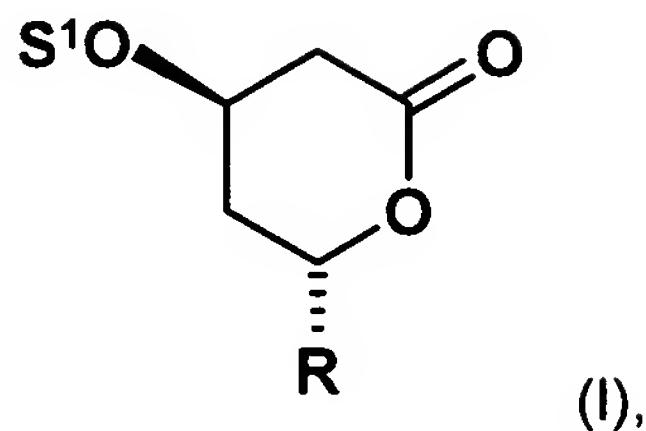
$R^8$  denotes  $-CH=P(R^3)_3$ ,  $-CH_2-P^+(R^3)_3M^-$ ,



15 where  $R^3$ ,  $R^4$ ,  $R^5$  and M are as defined in Claim 1,

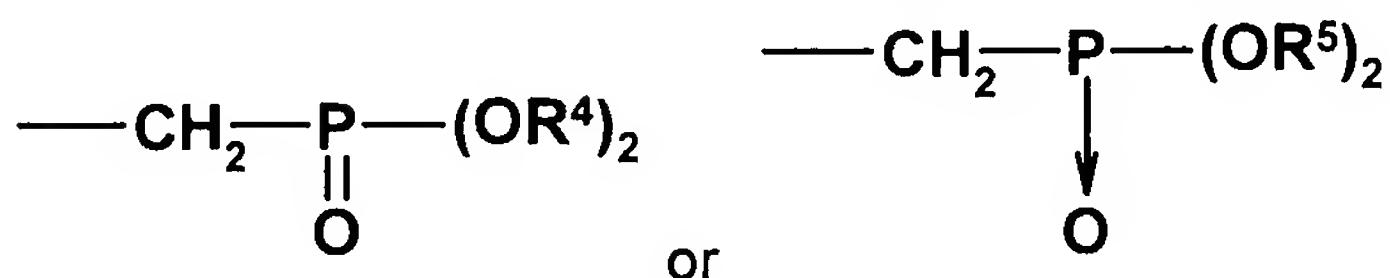


b) reaction of a compound of the formula I



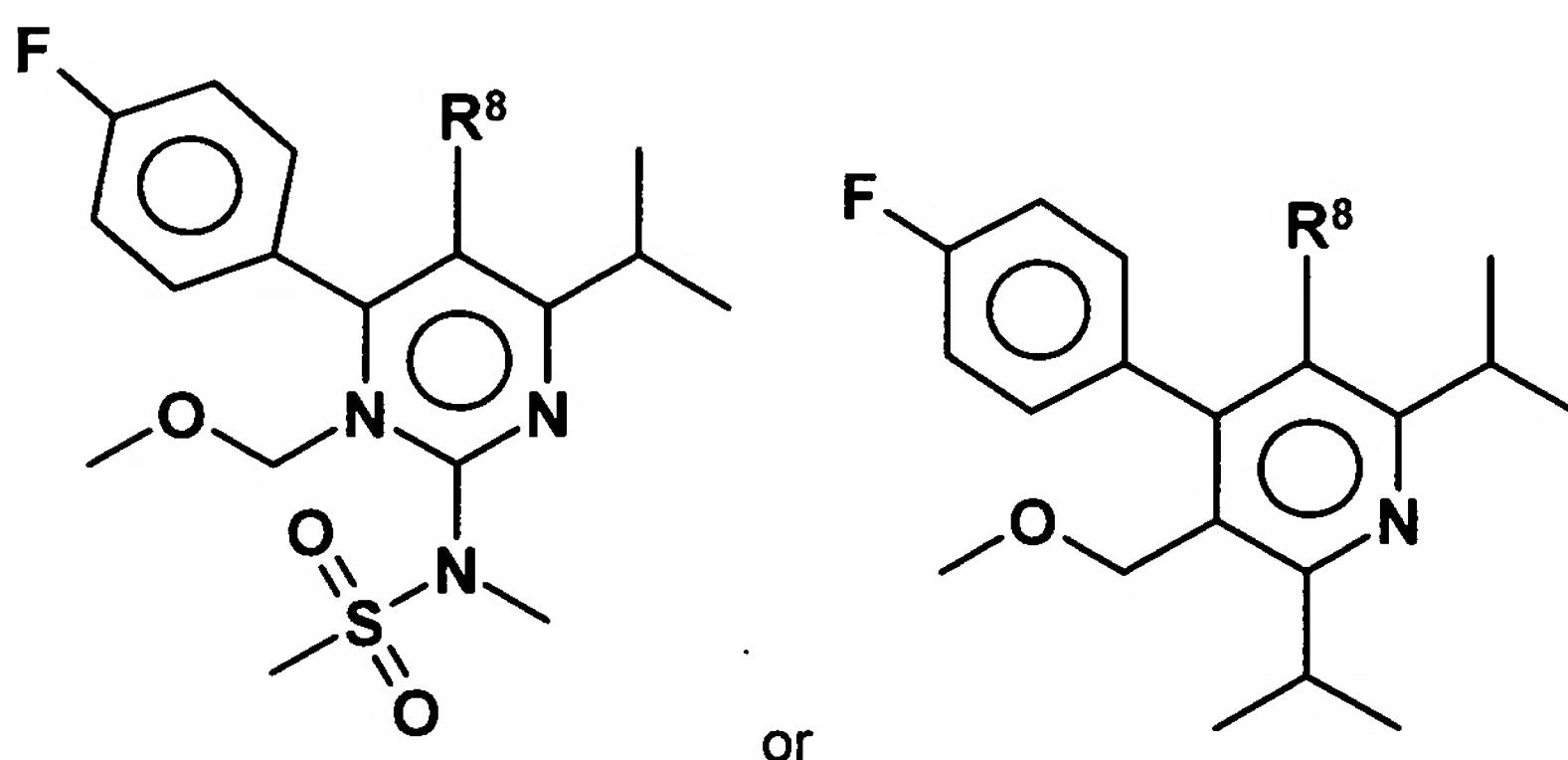
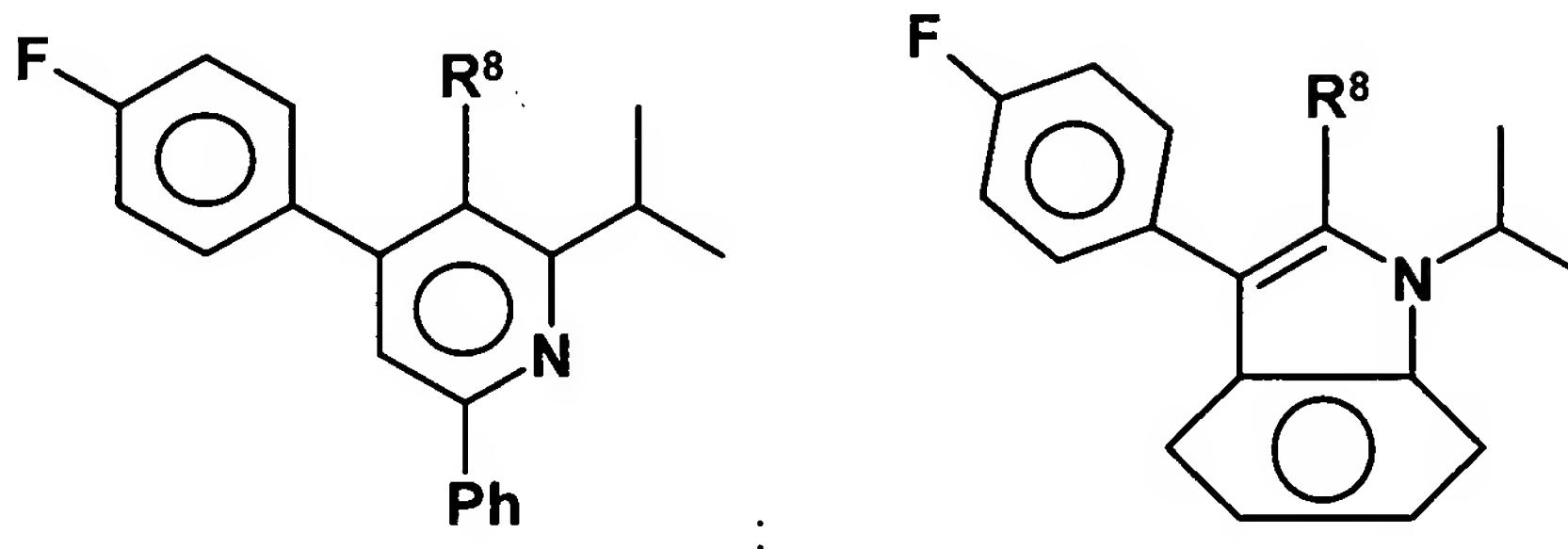
5 in which

the radical R denotes  $-\text{CH}=\text{P}(\text{R}^3)_3$ ,  $-\text{CH}_2-\text{P}^+(\text{R}^3)_3\text{M}^-$ ,



with a compound of the formula

10

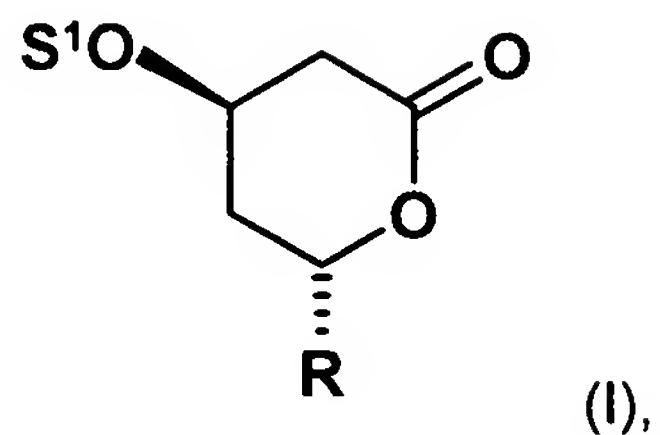


in which

15  $\text{R}^8$  denotes  $-\text{CHO}$ ,

where  $R^3$ ,  $R^4$ ,  $R^5$  and  $M$  are as defined in Claim 1,

c) reaction of a compound of the formula I



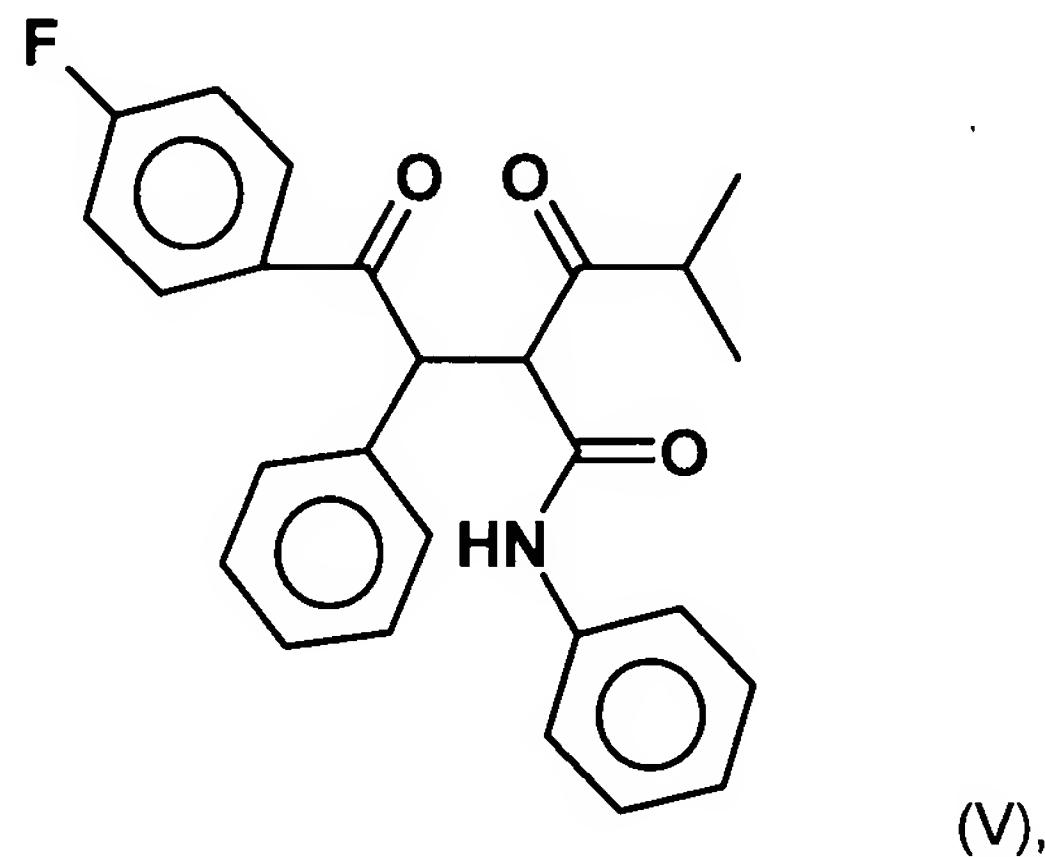
5 in which

the radical R is a group -CH<sub>2</sub>-C≡N,

Hydrogenation of the compound of the formula I in which the radical R is a group -CH<sub>2</sub>-C≡N, to give a compound of the formula I in which the radical R is a group -CH<sub>2</sub>-CH<sub>2</sub>NH<sub>2</sub>,

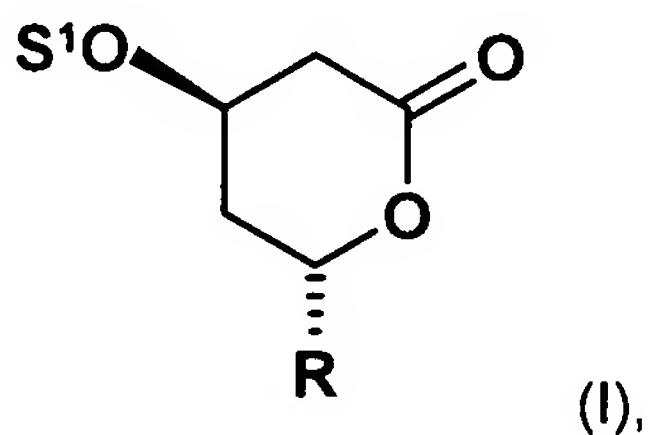
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and reaction of the compound of the formula I in which the radical R is a group -CH<sub>2</sub>-CH<sub>2</sub>NH<sub>2</sub> with a compound of the formula V



15

d) hydrogenation of a compound of the formula I

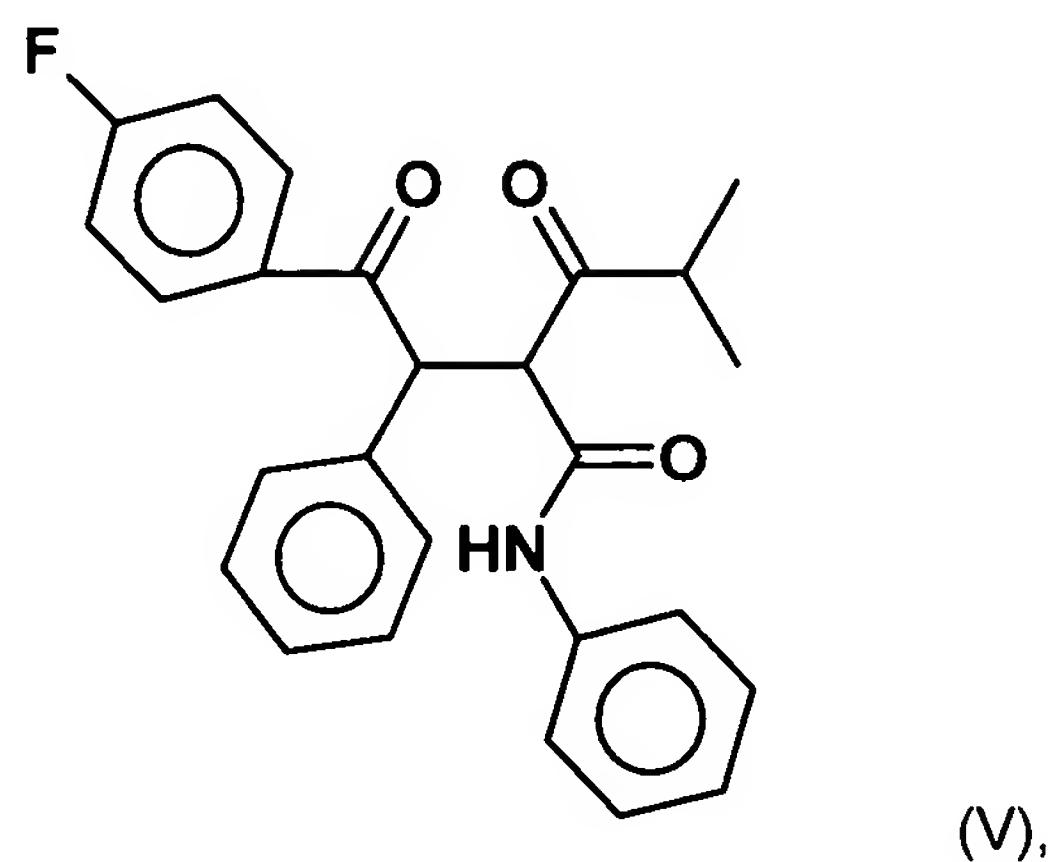




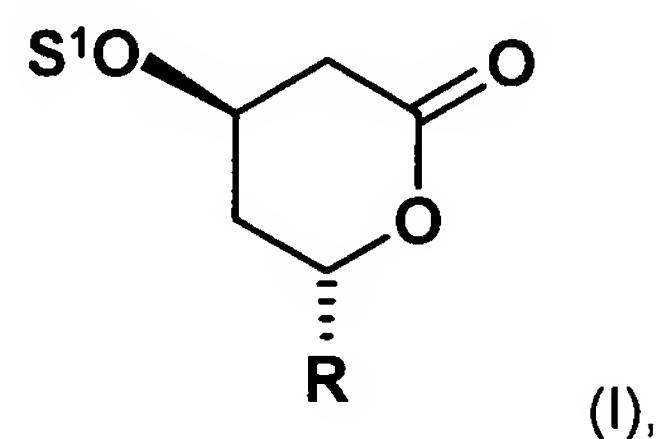
in which

the radical R is a group -CH<sub>2</sub>-C≡N, to give a compound of the formula I in which the radical R is a group -CH<sub>2</sub>-CH<sub>2</sub>NH<sub>2</sub>,

5 and reaction of the compound of the formula I in which the radical R is a group -CH<sub>2</sub>-CH<sub>2</sub>NH<sub>2</sub> with a compound of the formula V

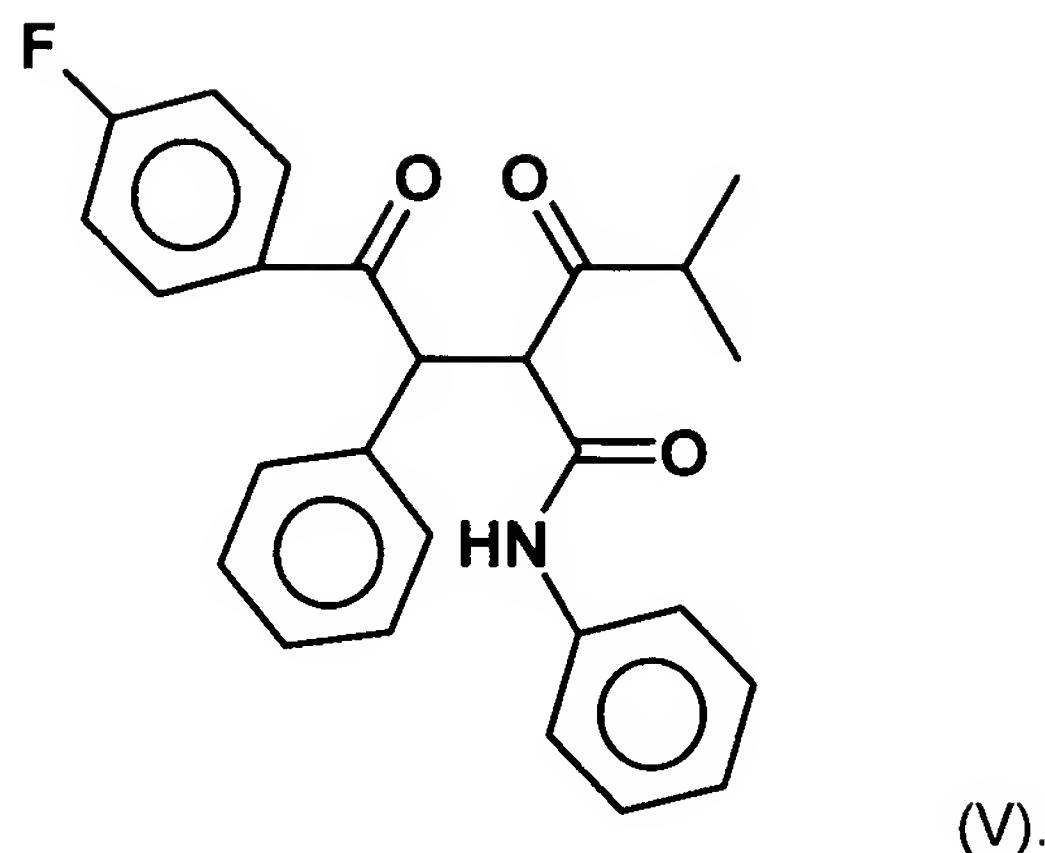


10 e) reaction of a compound of the formula (I)



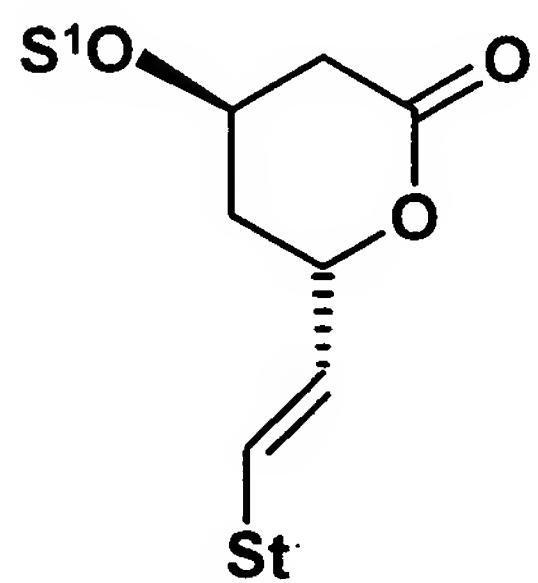
in which

15 the radical R is a group -CH<sub>2</sub>-CH<sub>2</sub>NH<sub>2</sub>, with a compound of the formula V



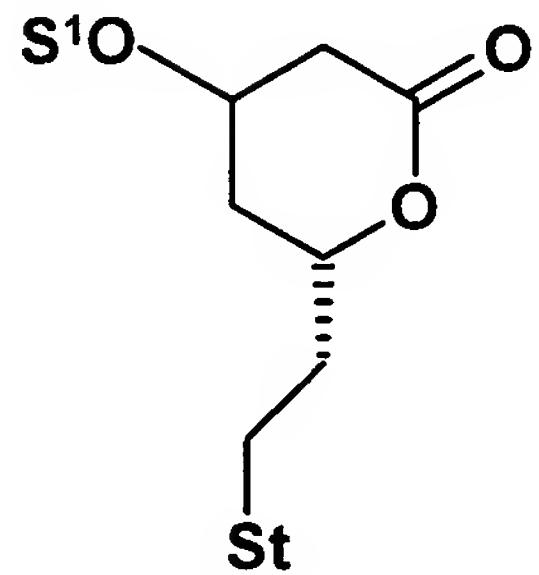
5. Process according any of Claims 1 to 4, characterized in that a compound of the formula

5



in which  $S^1$  is as defined in Claim 1 and  $St$  represents the radical of the statin, is converted into a compound of the formula

1.0



by catalytic hydrogenation, and optionally the protective group  $S^1$  is removed and optionally the lactone ring is opened.

15

6. Process according to any of Claims 1 to 5, the hydroxyl protective group S<sup>1</sup> being selected from a trimethylsilyl, triisopropylsilyl, trimethylsilylethyl, tert-butyldimethylsilyl, tert-butylmethylsilyl, di-tert-butylmethylsilyl, tert-butyldiphenylsilyl, triphenylsilyl, diphenylmethylsilyl, tris(trimethylsilyl) and para-tosyl protective group.

5

7. Process according to any of Claims 1 to 6, the protective groups S<sup>2</sup> and S<sup>3</sup> being bridged.

8. Process according to Claim 7, the protective groups S<sup>2</sup> and S<sup>3</sup> together representing an isopropylidene protective group.

9. Process according to any of Claims 2 to 7, the radical R representing a radical CH<sub>2</sub>R<sup>2</sup> and R<sup>2</sup> representing a leaving group, the leaving group being selected from a halogen atom and a radical -OSO<sub>2</sub>-C<sub>1</sub>-C<sub>6</sub>-alkyl or -OSO<sub>2</sub>-C<sub>5</sub>-C<sub>10</sub>-aryl.

15

10. Process according to any of Claims 1 to 9, the radical R<sup>1</sup> denoting a hydrogen atom or a C<sub>1-3</sub>-alkyl or C<sub>4-10</sub>-aryl radical, which are optionally substituted by one or more radicals, which, independently of one another, are selected from halogen atoms, heterocycles which have 0 to 10 carbon atoms and 1 to 10 heteroatoms selected from sulphur, nitrogen and oxygen atoms, and functional groups.

20

11. Process according to any of Claims 1 to 10,

R<sup>3</sup> denoting a C<sub>5</sub>- to C<sub>10</sub>-aryl radical which is optionally substituted by one or two C<sub>1</sub>-C<sub>4</sub>-alkyl radicals and/or halogen atoms, a C<sub>1</sub>-C<sub>4</sub>-alkyl radical or a C<sub>5</sub>-C<sub>10</sub>-cycloalkyl radical,

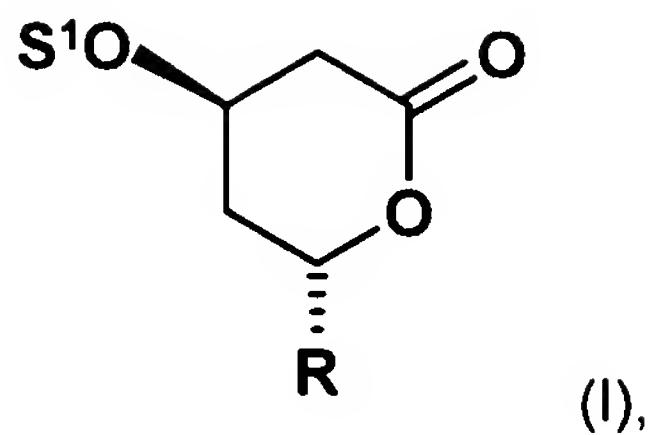
25 R<sup>4</sup> denoting a C<sub>1</sub>-C<sub>4</sub>-alkyl radical,

R<sup>5</sup> denoting a C<sub>1</sub>-C<sub>6</sub>-alkyl or C<sub>5</sub>-C<sub>10</sub>-aryl radical.

12. Process according to any of Claims 1 to 11, the statin being fluvastatin, rosuvastatin, cerivastatin, glenvastatin or atorvastatin.

30

13. Compound of the formula I

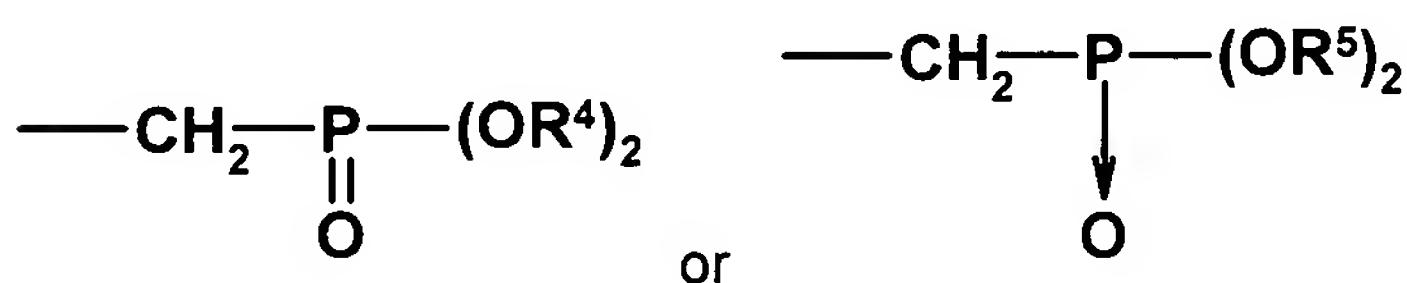


in which

$S^1$  and  $R$  are as defined in Claim 2, with the proviso that the radical  $S^1$  does not represent a 5 tert-butyldimethylsilyl group if the radical  $R$  represents a CHO, -CH<sub>2</sub>-OTos, -CH<sub>2</sub>Cl or -CH<sub>2</sub>I group.

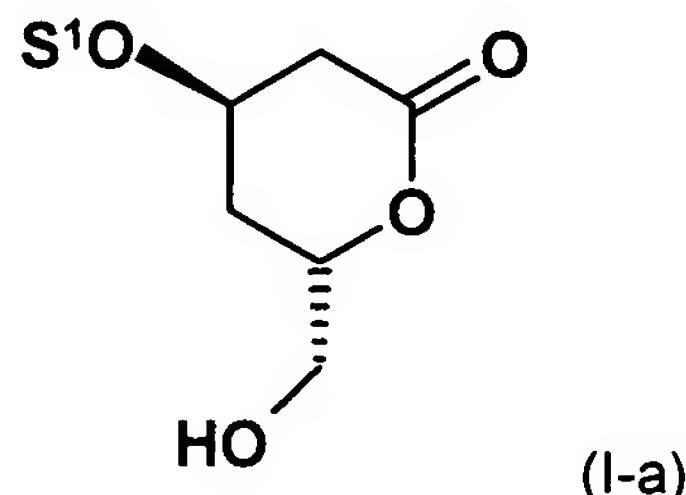
14. Compound according to Claim 13, in which the radical  $S^1$  represents a tert-  
butyldimethylsilyl group and the radical  $R$  represents a -CH<sub>2</sub>R<sup>2</sup>, -CH=P(R<sup>3</sup>)<sub>3</sub>, -CH<sub>2</sub>-P<sup>+</sup>(R<sup>3</sup>)<sub>3</sub>M<sup>-</sup>,

10



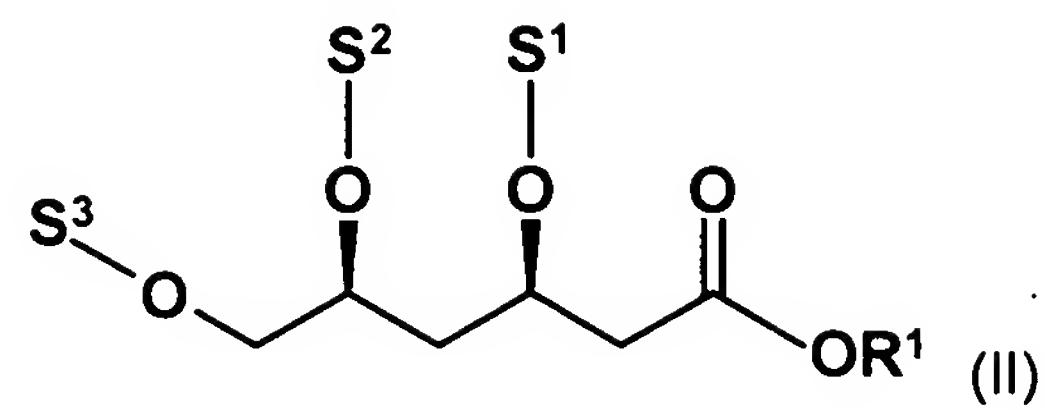
or group, where  $R^2$  represents a bromine atom, a -C≡N, a -CH<sub>2</sub>NH<sub>2</sub> group or a radical -SO<sub>2</sub>-R<sup>6</sup>, and R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and M are as defined in Claim 2.

15 15. Process for the preparation of a compound of a formula (I-a)



in which the radical  $S^1$  is as defined in Claim 1, characterized in that a compound of the formula II

20



in which

S<sup>1</sup>, S<sup>2</sup>, S<sup>3</sup> and R<sup>1</sup> are as defined in Claim 1, is converted into the compound of the formula I-a  
5 by lactonization.